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02-1434, 02-1459

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

APPLERA CORPORATION,
MDS INC., and APPLIED BIOSYSTEMS/MDS SCIEX,

Plaintiffs-Appellees,

v.

MICROMASS UK LTD. and MICROMASS INC.,

Defendants-Appellants.

Appeal from the United States District Court for the District of Delaware
in Case 00-CV-105, Judge Roderick R. McKelvie

REPLY BRIEF OF APPELLANTS MICROMASS UK LTD. AND MICROMASS INC.

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October 25, 2002

district court's construction disregards the differences between these two paragraphs and renders *located end to end* merely redundant with the express limitations of paragraph (d).

In sum, the district court's contrived construction finds no basis in the specification or plain meaning of *located end to end*, has the effect of eviscerating this limitation, and must have been improperly influenced by the structure of the accused products.

2. The District Court's Unsupported Constructions Of *Separated By A Wall* And *Interchamber Orifice* Must Also Be Reversed

Micromass seeks a construction of *separated by a wall* and *interchamber orifice* that is consistent with plain meaning and the specification, not to limit the claims to the preferred embodiments. *Bell Atlantic,* 262 F.3d at 1273 (usage of "preferred" does not broaden the claims beyond their support in the specification); *Netword, LLC v. Centraal Corp.,* 242 F.3d 1347, 1352 (Fed. Cir. 2001) ("[a]lthough ... the claims are not limited to the preferred embodiment of the invention ... neither do the claims enlarge what is patented beyond what the inventor has described as the invention").

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distinguishable. There, the patentee did not seek a claim construction similar to other language in the claim.

With respect to *separated by a wall,* the issue is whether "a wall" is singular or permits multiple walls. While the indefinite article "a" or "an" can mean "one or more," the methodology followed by this Court is to determine from the remaining claim language and specification whether a plural or singular meaning was intended by the inventors. *Abtox, Inc. v. Exitron Corp.,* 122 F.3d 1019, 1023 (Fed. Cir. 1997).

In *Abtox*, the disputed claim limitation recited "a metallic gas-confining chamber." Other limitations recited structures "within said chamber." The Court found "this language clarifies that only one chamber is in question." *Abtox,* 122 F.3d at 1024. The Court further relied upon the patent figures, which showed a single chamber, and the fact that "[n]othing in the written description suggests that the claim language encompasses a device with more than one gas-confining chamber." *Id.*; *see also Insituform Technologies, Inc. v. Cat Contracting, Inc.*, 99 F.3d 1098, 1105-06 (Fed. Cir. 1996) (because "nothing in the text of claim 1 suggests the use of more than one cup," and "neither the specification nor the drawings disclose the use of more than one cup," the only correct interpretation is that the claim is limited to a single cup).

Here, as in *Abtox,* the claim places the interchamber orifice specifically "in said wall," *i.e.,* the wall that separates the first and second vacuum chambers.

(A362 at 14:25-26, 14:45.) The usage of "said wall" reinforces the singular nature of "a wall." *Abtox,* 122 F.3d at 1024.

Further, the phrase *separated by a wall* itself requires a single wall. For example, if someone were to say that "the Judge's chambers and his secretary's office are *separated by a wall*," then everyone would understand that the chambers and office are next to each other and there is a single wall between them. On the other hand, the statement "Courtrooms 201 and 203 are *separated by a wall*," is literally incorrect because there are several walls and a hallway between the two courtrooms. Thus, the ordinary meaning of *separated by* requires a single wall, because if there were two or more walls, none of them would *separate* the first and second vacuum chambers.

Moreover, the patent drawings and written description uniformly teach a single wall between the first and second vacuum chambers. Therefore, because nothing in the language of the claims or the specification suggests that *a wall* has anything other than its "normal singular meaning," the phrase must be so interpreted. *North American Vaccine, Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 1576 (Fed. Cir. 1993); *Abtox,* 122 F.3d at 1024; *Insituform,* 99 F.3d at 1105-06.[4]

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[4] *Crystal Semiconductor Corp. v. Tritech Microelectronics Int'l, Inc.* 246 F.3d 1336 (Fed. Cir. 2001), is readily distinguished. The disputed limitation was

Finally, there has been no waiver with respect to the construction of *separated by a wall*. Micromass proposes a claim construction that has the same scope as the construction it advocated in the district court. (A8835-37 ("[t]he first and second vacuum chambers are separated *only* by a wall").) *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1346 (Fed. Cir. 2001) (claim construction is "new" only if it changes the scope). Micromass is permitted to make new or additional arguments in support of that same claim construction. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1371 (Fed. Cir. 2002) ("[a] waiver will not necessarily occur ... if a party simply presented new or additional arguments in support of the 'scope of its claim construction' on appeal") (quoting *Interactive,* 256 F.3d at 1347). In any event, the district court record leaves no doubt that Micromass opposed AB/Sciex' proposed construction, which was adopted by the district court. (A8695-97, A10000-01.)

With respect to *interchamber orifice,* the issue is whether the district court correctly omitted the "interconnecting" requirement from its construction.

"a third ... layer disposed over a portion of said second ... layer." *Id.* at 1346. The Court held that "a portion" meant "at least one portion" because "the written description *require[d]* claim 1 to encompass a ... structure wherein the third layer covers the entirety of the second layer." *Id.* at 1349 (emphasis added). In contrast, nothing in the '736 patent specification suggests, let alone *requires,* that the claims encompass a structure having more than one wall.

Whenever a claim is construed, the meaning of the claim language must necessarily be defined using words not found in the claim. In this regard, there is no distinction between the word, "between," which AB/Sciex agrees can be read into the claim, and "interconnecting," which AB/Sciex contends cannot. Neither is found in the claims. On the other hand, the specification describes the first and second chambers as "connected" by the interchamber orifice, but nowhere describes the interchamber orifice as merely "between" these chambers. (A357 at 4:24-26.)

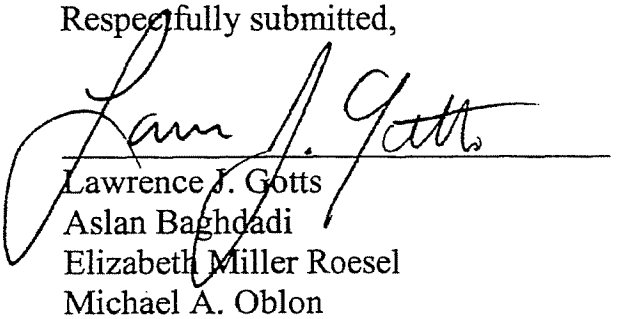
Moreover, the claims require that the interchamber orifice is "in said wall" such that it interconnects not just any two chambers, but the first and second vacuum chambers that are "separated by a wall." Accordingly, consistent with the language of the claims as a whole and the broadest description in the specification, the *interchamber orifice* must be construed as an orifice that is not merely between, but also *interconnecting* the first and second vacuum chambers. *Netword,* 242 F.3d at 1352 ("[t]he claims are directed to the invention that is described in the specification; they do not have meaning removed from the context from which they arose").

IV. CONCLUSION

For all of the foregoing reasons and those set forth in Micromass' principal brief, the judgment of the district court must be reversed.

October 25, 2002

Respectfully submitted,



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IN THE UNITED STATES DISTRICT COURT

IN AND FOR THE DISTRICT OF DELAWARE

APPLERA CORPORATION, MDS, INC., and APPLIED BIOSYSTEMS/MDS SCIEX, Plaintiffs vs. MICROMASS UK LTD. and MICROMASS, INC., Defendants

CIVIL ACTION

NO. 2000-105 (RRM)

- - -

Wilmington, Delaware
Thursday, December 13, 2001
2:00 o'clock, p.m.

- - -

BEFORE: HONORABLE RODERICK R. McKELVIE, U.S.D.C.J.

- - -

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PROCEEDINGS

(Proceedings commenced in the courtroom, beginning at 2:00 p.m.)

THE COURT: Good afternoon.

Shall we do some introductions first?

MS. HEANEY: Good afternoon, your Honor. Julie Heaney, for the plaintiff.

We have Walter Hanley, Jim Galbraith, Lewis Popovski and Huiya Wu and Jeffrey Ginsberg, of Kenyon & Kenyon.

THE COURT: Okay. Good afternoon.

MR. WHETZEL: Your Honor, Bob Whetzel, for defendant Micromass.

We're outnumbered by a few, but with me is Jim Hunter, Ken Schuler and Kevin May, from Latham.

I'd also like to introduce some representatives of Micromass that are in the back of the courtroom. Mr. Bob Williams, who's Chairman of Micromass, Mr. Norman Lynaugh, who's a Managing Director, David Yorke, who's the I.P. Manager for Micromass.

THE COURT: Nice to see everybody.

MR. HANLEY: Your Honor, just one more. I'd

be remiss in not according the AB/Sciex representative. Also, we have Andrew Karnakis, who's patent counsel at AB/Sciex.

THE COURT: Good.

So why don't I get two victims up and we'll talk about what we want to do and how we want to do it. And that lectern is only there because the lawyers during closing argument end up leaving it there. Usually, it floats back over here.

In light of current conditions, meaning the fact that I bumped you out of this morning to this afternoon, and that we have a number of things to get done, let me make some suggestions, and then we'll see whatever suggestions you have about it. My thought is that we do claim construction and then, to the extent that we have time left over, we'll let people pick a topic that they'd like to address and we'll just go back and forth on topics.

We're not going to get everything done today. I know we've got a trial coming up, pretrial conference coming up, and at least from my perspective the priority is going to be to get claim construction done, get an opinion out as soon as I can and to offer the suggestion we get back together as soon as I get claim construction out and have further argument and see what the claim

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And now what do they say in this case? Having said in the -- I mean, subsequent to the Interrogatory Answer, 133. Yes, 133 will do.

No. I take that back. Let's go to 129.

Same response after final office action. The first space could be at an angle relative to the second space and the two spaces could be aligned by having the ends precisely located relative to each other so that their ends -- so that -- so that -- guess what? So that their ends abut.

Now, 133. Interrogatory Answer said it means axially aligned. Re-examination proceeding says, no, no, it does not mean that, because they just have to have the ends abut. They can be at an angle. Now what do they say? Located end to end means positioned so as to align the spaces. The word axially is no longer there, defined by the first and second rod sets. But if that's what it means, then end to end does not mean anything because the claim already requires without end to end in it that said first and second spaces are aligned.

They are attempting to read end to end...

(Pause.)

THE COURT: Go ahead.

MR. HUNTER: Thank you, your Honor.

They are attempting -- and that's exactly what

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this does -- they are attempting to read end to end out of the patent. And the reason that they're attempting to read end to end out of the PATENT and get themselves in this mix, where they say axially aligned in an Interrogatory Answer in this case, and then they have to back off that because we show that it's inconsistent with the fact that they can abut and be at an angle in the re-examination proceeding, the reason they want to read it out is because end to end requires that the two rod sets be located so that their ends are next to each other. And if that's the case, the Quattro Ultima does not infringe, because what they accuse as the first rod set in the Quattro Ultima is the first rod set, albeit in the second vacuum chamber, but the second rod set, the very first AC/DC rod set in the Quattro Ultima, is the fourth rod set, and it is separated from the first rod set, as you will see in our papers, by an -- by a wall, by another AC/DC rod set, by another wall, and by another AC/DC rod set.

You don't get from what they say is the first rod set in our Quattro Ultima for infringement purposes to the next one, which they say is the second one, until you go through two other AC/DC rod sets and two walls. That's why they want to read it out.

But notice, our construction of end to end; namely, that the two have to be next to each other, is

Page 91

consistent not only with the plain meaning of end to end, it's consistent with the plain meaning of first and second.

136. And it is the one that permits both configurations, which there are other claims specifically the same are allowed as dependent claims.

Our construction permits both. And it's consistent with the meaning of end to end and consistent with the meaning of first and second, and is the only one that does that, your Honor.

Next?

Interchamber orifice. Does the same thing.

Next?

Claim 1A and D together. First and second vacuum chambers separated by a wall, an interchamber orifice located in said wall and aligned with said first and second spaces.

41. Not just separated, separated by.

Back to 39.

First and second spaces separated by an interchamber orifice.

Back to 38.

First and second vacuum chambers separated by a wall containing an interchamber orifice. Separated by, not just separated.

Page 92

If I were to say to somebody that President Bush's Oval Office is separated from his secretary by a door, everybody would know what separated by means. It means there's a door between President Bush and his secretary's office. They are next to each other.

But if I were to say that this courtroom is separated from the oval office by that door (indicating), people would say I was nuts. This claim language requires that the first and second vacuum chambers be separated by a wall containing an interchamber orifice.

Next?

This claim language requires that the first and second spaces be separated by an interchamber orifice. Not just separated from each other, but separated by an interchamber orifice.

42?

Claim 14B goes on and said directing said ions through inlet orifice into the first space, first through said first space, said interchamber orifice and then through said second space.

Next?

Then through said second space next in order of time, walked to the door, then turned, or following next after in order of position, next after. First came the clowns, then came the elephants.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

APPLERA CORPORATION, MDS INC., and APPLIED BIOSYSTEMS/MDS SCIEX INSTRUMENTS Plaintiffs, v. THERMO ELECTRON CORPORATION, Defendant and Counter-Plaintiff.	Civil Action No: 04-1230-GMS

DEFENDANT THERMO ELECTRON CORPORATION'S SECOND SUPPLEMENTAL RESPONSES TO PLAINTIFFS' FIRST SET OF INTERROGATORIES (NOS. 1-15)

[Douglas Patent]

Pursuant to Rules 26 and 33 of the Federal Rules of Civil Procedure, Defendant and Counter-Plaintiff Thermo Electron Corp. ("Thermo") further responds to the First Set of Interrogatories by Applera Corp., MDS Inc., and Applied Biosystems/MDS Sciex Instruments (together "Applera") as follows:

GENERAL OBJECTIONS

Unless otherwise indicated, Thermo will not provide an answer to any interrogatory, or to any sub-part thereto, encompassed by the following objections.

1. Thermo objects to any interrogatory that seeks information protected from disclosure by the attorney-client privilege, the attorney work product doctrine, the joint defense or common interest privilege, or any other applicable privilege or immunity. The inadvertent

Response to Interrogatory No. 8:

Thermo objects to this interrogatory because it is compound, containing at least two separate questions. Thermo objects to this interrogatory because it is premature. Thermo objects to this interrogatory to the extent that it seeks information protected from disclosure by the attorney-client privilege and the attorney work product doctrine. Subject to the foregoing general and specific objections, Thermo answers as follows:

Thermo first became aware of the '736 patent in approximately late 1990 or early 1991. It was (and is) Thermo's business to stay informed about patents that issue in the field of mass spectrometry, and Thermo became aware of the patent in the ordinary course of its business. Thermo cannot fairly identify "one" person or group of people who first became aware of the patent. There have been various design changes, actual and contemplated, to the Accused Mass Spectrometers over time. Among the considerations that are part of the design process is the desire to avoid infringing the intellectual property of others. All design changes are made to enhance the operation of the machines. Thermo is unaware of any change that was made particularly to avoid or "design around" the '736 patent.

Interrogatory No. 9:

For each Accused Mass Spectrometer that Defendant contends does not infringe the '736 patent, identify each and every claim limitation that is missing from such product, describe each and every fact that forms the basis for such non-infringement contention, and identify each and every document that supports or tends to support each such fact.

Response to Interrogatory No. 9:

Thermo objects to the request to "describe each and every fact" and to "identify each and every document" as overbroad and unduly burdensome. Thermo objects to this request because certain of the asserted claims are method claims, which cannot be infringed by a "product." Thermo objects to this interrogatory as premature. Subject to the foregoing general and specific objections, Thermo answers as follows:

The Accused Mass Spectrometers do not satisfy the claimed elements (literally or equivalently) of any asserted claim of the '736 patent. The Accused Mass Spectrometers would not satisfy a number of claim elements. For example, the Accused Mass Spectrometers lack the requirement of Claim 1 of "first and second vacuum chambers separated by a wall, said first vacuum chamber having an inlet orifice therein," and each of such chambers containing a "rod set" "comprising a plurality of elongated parallel rod means." As all lettered limitations of Claim 1 depend on that initial structure, the Accused Mass Spectrometers also do not satisfy the lettered limitations of Claim 1. As a specific example, the Accused Mass Spectrometers do not satisfy the requirement of a specified product of pressure times length being equal to or greater than 2.25×10^{-2} torr cm "whereby to provide improved transmission of ions."

The Accused Mass Spectrometers do not meet the limitation of claims 2-6.

The Accused Mass Spectrometers do not contain the limitation "wherein said means for controlling the kinetic energy of said ions comprises means for applying a low DC voltage between said first rod set and said inlet wall" of claim 8.

The Accused Mass Spectrometers do not contain the limitation "wherein said means for controlling the kinetic energy of said ions comprises means for applying a low DC voltage between said first rod set and said inlet wall, said low DC voltage being between 1 and 30 volts DC" of claim 9.

The Accused Mass Spectrometers do not contain the limitation "wherein said means for controlling the kinetic energy of said ions comprises means for applying a low DC voltage between said first rod set and said inlet wall, said low DC voltage being between 1 and 15 volts DC" of claim 10.

The Accused Mass Spectrometers do not contain the limitation "wherein said means for controlling the kinetic energy of said ions comprises means for applying a low DC voltage between said first rod set and said inlet wall, said low DC voltage being between 1 and 10 volts DC" of claim 11.

For the reasons stated above, Thermo cannot provide an answer as to Claim 14, which is a method claim that cannot be practiced by a "product." Subject to and without waiving the general and specific objections set forth above, Thermo states that the Accused Mass Spectrometers do not contain a "first rod set and a second rod set located in first and second vacuum chambers respectively, said first and second rod sets each comprising a plurality of rod means." As all lettered limitations of Claim 14 depend on that initial structure, the Accused Mass Spectrometers also do not satisfy the lettered limitations of Claim 14. As a specific example, the Accused Mass Spectrometers do not satisfy the requirement of a specified product of pressure times length being equal to or greater than 2.25×10^{-2} torr cm "whereby to provide improved transmission of ions." Thermo cannot provide a response to the assertion of claims 15-19, 21-24, and 27, 29, and 30 because these are method claims that cannot be practiced by a "product" or machine by itself.

In addition, the LTQ series mass spectrometers do not have a "mass filter." The absence of a mass filter means that the LTQ series mass spectrometers also do not meet several other limitations in the claims of the '736 patent. In addition, the LTQ series mass spectrometers do

not apply a DC voltage "between the rods" in the mass analyzer. As pertinent to this part of the patent claims, the machines in the LTQ series only apply an AC voltage between the rods.

Interrogatory No. 10:

Describe in detail each and every fact that supports or tends to support Defendant's contention that one or more claims of the '736 patent are invalid including, without limitation, a description of each and every fact that formed the basis of such contention.

Response to Interrogatory No. 10:

Thermo objects to the request for "each and every fact" as overbroad and unduly burdensome. Thermo objects to this interrogatory as premature. Subject to the foregoing general and specific objections, Thermo answers as follows:

Thermo is aware that in litigation against Plaintiffs, Micromass UK Ltd. and Micromass Inc. asserted several theories as to the invalidity of the '736 patent. Thermo is aware that Micromass Ltd. has filed an opposition to the European counterpart of the '736 patent with the European Patent Office raising invalidity arguments. On March 29, 2005, Thermo Finnigan LLC filed Third-Party Observations in support of the Micromass opposition.

In addition, Thermo states that the following references, individually or in combination, render the '736 patent invalid:

1. Scott L. Anderson & Luke Hanley, *Metal Cluster Ion Chemistry*, SPIE, vol. 669 (Laser Applications in Chemistry), pp. 133-136 (1986).
2. C.A. Boitnott, J.R.B. Slayback & U. Steiner, *Optimization of Instrument Parameters for Collision Activated Decomposition (CAD) Experiments for a Triple Stage Quadrupole (TSQ™) GC/MS/MS/DS*, Finnigan MAT, Finnigan Topic 8160 (1981).
3. Charles A. Boitnott, Urs Steiner & John R.B. Slayback, *Optimization of Instrument Parameters for Collision Activated Decomposition (CAD) Experiments for a Finnigan Triple Stage Quadrupole GC/MS/MS/DS*, Abstracts, 1981 Pittsburgh Conference, no. 782 (1981).

Response to Interrogatory No. 15:

Thermo objects to the request for "each person" as overbroad and unduly burdensome. Subject to the foregoing specific and general objections, Clay Campbell, Jae Schwartz, and Iain Mylchreest gathered and supplied information used in preparing the responses to the above interrogatories.

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Dated: December 2, 2005

LEXSEE

NOVO NORDISK A/S and NOVO NORDISK PHARMACEUTICALS INC., Plaintiffs, v. ELI LILLY AND COMPANY, Defendant. ELI LILLY AND COMPANY, Counterclaim Plaintiff, v. NOVO NORDISK A/S, NOVO NORDISK PHARMACEUTICALS INC., and NOVO NORDISK OF NORTH AMERICA, INC., Counterclaim Defendants.

Civil Action No. 98-643 MMS

UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE

1999 U.S. Dist. LEXIS 18690

October 6, 1999, Argued
November 18, 1999, Decided

NOTICE: [*1] FOR ELECTRONIC PUBLICATION ONLY

CASE SUMMARY:

PROCEDURAL POSTURE: Plaintiffs sought a declaratory judgment that defendant's patent was invalid, unenforceable, and had not been infringed upon by plaintiffs; and defendant counterclaimed against plaintiffs for infringement of the patent. At issue in the suit was the scope and meaning of certain language in the patent claims.

OVERVIEW: Plaintiffs sought a declaratory judgment that defendant's patent was invalid, unenforceable, and had not been infringed upon by plaintiffs. Defendant counterclaimed against plaintiffs for infringement of the patent. The parties disagreed on the scope and meaning of certain claim language. Therefore, the court construed the scope and meaning of the disputed claim language. The patent at issue related to insulin and insulin analogs and their use in the treatment of diabetes mellitus. The court held that the proper construction of claims was based primarily on intrinsic evidence, i.e., the claim language, the specification, and the prosecution history; that intrinsic evidence supported the court's definitions of the disputed terms: "complex," "hexamer," and "formulation." Moreover, because these definitions were clear from the intrinsic evidence of the patent, the court held that it was unnecessary and improper to examine the extrinsic evidence proffered by the parties.

OUTCOME: The court construed the scope and meaning of the disputed claim language, but did not reach the point of comparing the claims with the allegedly infringing device. The court held that its construction of the disputed claim language was supported by intrinsic evidence, so it would not consider extrinsic evidence.

CORE TERMS: hexamer, insulin, molecule, equilibrium, analog, zinc, ion, specification, pharmaceutical, molecular, patent, formulated, patient, phenolic, parenteral, invention, monomeric, conformation, rapid, dictionary, hexameric, phenol, injection, monomer, stable, consisting, polymer, subcutaneous, comprise, m-cresol

LexisNexis(R) Headnotes

Patent Law > Infringement Actions > Claim Interpretation > Fact & Law Issues
Patent Law > Infringement Actions > Claim Interpretation > Scope
[HN1] Patent infringement actions are composed of two phases. First, in the claim construction, or Markman, phase, the federal district court determines the scope and meaning of the patent claims as a matter of law. Second, the claims are compared to the allegedly infringing device.

Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN2] The proper construction of claims is based primarily on the intrinsic evidence: the claim language, the specification, and the prosecution history. Claims shall be construed from the point of view of a person of ordinary skill in the field of the invention, at the time of the invention.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN3] The claim language itself is first and foremost in importance when construing the meaning and scope of a patent.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN4] The general rule for interpreting the language of a claim is that terms in the claim are to be given their ordinary and accustomed meaning. General descriptive terms will ordinarily be given their full meaning; modifiers will not be added to broad terms standing alone. In short, a federal district court must presume that the terms in the claim mean what they say, and, unless otherwise compelled, give full effect to the ordinary and accustomed meaning of claim terms. Thus, if the claim is unambiguous and clear on its face, the district court need not consider the other intrinsic evidence.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN5] Where the applicability of a common meaning is unclear or where more than one common meaning can be assigned to a claim term, reference to the specification and prosecution history is appropriate to discern the ordinary and accustomed meaning. Thus, the claims are construed in accordance with the rest of the specification of which they are a part, and not contrary to it. Indeed, the construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN6] A federal district court engaging in claim construction may enter a definition of a claim term other than its ordinary and accustomed meaning in two situations. The first arises if the patentee has chosen to be his or her own lexicographer by clearly setting forth an explicit definition for a claim term in the specification. The second is where the claim term or terms chosen by the patentee so deprive the claim of clarity that there is no means by which the scope of the claim may be ascertained from the language used. In these two circumstances, a term or terms used in the claim invites -- or indeed, requires -- reference to intrinsic evidence beyond the claim language itself, or in some cases, extrinsic evidence to determine the scope of the claim language.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN7] The specification has been described as often the single best guide to the meaning of a disputed term. When the specification explains and defines a term used in the claims, without ambiguity or incompleteness, there is no need to search further for the meaning of the term. At the same time, however, a federal district court may not read a limitation into a claim from the written description.

Patent Law > U.S. Patent & Trademark Office Proceedings > Continuation Applications > General Overview

Patent Law > Infringement Actions > Prosecution History Estoppel > General Overview

Patent Law > Infringement Actions > Doctrine of Equivalents > General Overview

[HN8] The prosecution history informs the understanding of terms found in both the specification and the claim. Use of the prosecution history to interpret claim language is distinct from prosecution history estoppel, which is a limitation on the doctrine of equivalents. In most instances, the prosecution history is cited to refute an overly broad interpretation of a claim term put forth by the patentee.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN9] After examining the intrinsic evidence of a patent, if the meaning of the claim language is still ambiguous, a federal district court may consider extrinsic evidence, if necessary, to aid in the district court's understanding of the patent. However, if the meaning of a disputed claim term is clear from the intrinsic evidence -- the written record -- that meaning, and no other, must prevail; it cannot be altered or superseded by witness testimony or other external sources simply because one of the parties wishes it were otherwise.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN10] The Federal Circuit has ranked four common forms of extrinsic evidence from most reliable to least reliable: (1) technical treatises and dictionaries; (2) prior art; (3) expert testimony on technology; and (4) expert testimony on claim construction. In some cases, reference to extrinsic evidence, although not necessary for claim construction, may have a useful confirmatory purpose.

Patent Law > Infringement Actions > Claim Interpretation > General Overview

[HN11] If a claim term is still ambiguous after the consideration of intrinsic and extrinsic evidence, a federal district court shall adopt the interpretation that affords more narrow coverage of allegedly infringing devices, so that the claims perform their intended function of giving notice of what is covered to potential infringers.

Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN12] Prevailing Federal Circuit law holds that dictionaries are extrinsic evidence. However, in a recent non-precedential decision, a diminished panel of the Federal Circuit holds that dictionary definitions are considered to be intrinsic evidence. Moreover, in several other cases, the Federal Circuit seems to employ a dictionary as part of its intrinsic analysis of the plain meaning of the claim language.

Patent Law > Claims & Specifications > Claim Language > Claim Transitions
Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN13] When used as a transition, the term "comprises" means that the claim is open-ended, so that it may include elements other than those explicitly recited in the claim.

Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN14] The expression of a limitation in one element of a claim implies the exclusion of that term in other elements of the claim. Moreover, each term in each claim must be given meaning.

Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN15] In the context of chemical patents, "consisting of" indicates closed claim language and closes the claim to the inclusion of unrecited elements, except for impurities ordinarily associated therewith.

Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN16] Interpreting what is meant by a word in a claim is not to be confused with adding an extraneous limitation appearing in the specification, which is improper.

Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN17] The prosecution history can only be used to understand the meaning of the terms in the claims, not to enlarge, diminish, or vary the limitations in the claims.

Patent Law > Infringement Actions > Claim Interpretation > General Overview
[HN18] The claims of a patent cannot be limited by disclosure of a preferred embodiment in the specification.

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JUDGES: Murray M Schwartz, Senior District Judge.

OPINIONBY: Murray M Schwartz

OPINION:

MEMORANDUM OPINION

Argued: October 6, 1999
Dated: November 18, 1999

SCHWARTZ, Senior District Judge

I. Introduction

Novo Nordisk A/S and Novo Nordisk Pharmaceuticals, Inc. (collectively "Plaintiffs") filed a complaint and amended complaint against Eli Lilly and Company ("Eli Lilly" or "Lilly") seeking a declaratory judgment that Lilly's U.S. Patent No. 5,474,978 ("the '978 patent"), entitled "Insulin Analog Formulations," is invalid, unenforceable, and not infringed by Novo Nordisk. Lilly counterclaimed against Plaintiffs and Novo Nordisk of North America, Inc. (collectively "Novo Nordisk" or "Novo") for infringement of the '978 patent.

The parties disagree on [*3] the scope and meaning of certain claim language. Pursuant to *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 134 L. Ed. 2d 577, 116 S. Ct. 1384 (1996), the Court now construes the scope and meaning of the disputed claim language in the '978 patent.

I. Factual Background

A. History of Insulin and Insulin Analogs

The '978 patent relates generally to insulin and insulin analogs and their use in the treatment of diabetes mellitus. Human insulin ("hI" or "insulin") is a naturally occurring human protein that performs the function of transporting sugar molecules from blood to cells where the sugar is needed for energy. Insulin is made up of 2 polypeptide chains (chain A and chain B) joined together by covalently bound n1 atoms of sulfur ("S"). n2

n1 A "covalent bond" is "a non-ionic chemical bond formed by shared electrons." Merriam-Webster's New Collegiate Dictionary 300 (10th ed. 1998).

n2 [SEE HUMAN INSULIN IN ORIGINALS]

Animals and humans having a deficiency of insulin [*4] suffer from a disease known as diabetes mellitus. They are dependent on injections of insulin to help regulate their blood sugar levels. However, it is difficult for diabetics to time these injections to avoid unhealthy fluctuations in blood sugar level, resulting in conditions known as hyper- and hypo-glycemia. Frequent fluctuations over the course of a lifetime can lead to long term complications such as hardening of the arteries, kidney failure, blindness, coma, and death.

Until the 1980's, human diabetics relied on injections of bovine, and other animal, insulin. In the 1980's, scientists developed methods to genetically engineer human insulin. This was a major advancement since hI works much better in humans than animal insulin. In solutions of pure hI, most of the molecules of hI exist as monomers, i.e., single molecules of hI. However, in that solution, the monomers of hI tend to rapidly form large, covalently bound polymers with one another. These polymers render the solution biologically inactive because hI will only act in the body in its monomeric form. It is very difficult for the covalently bound polymers to break apart and separate into monomers. Thus, solutions of monomers [*5] of hI have a very short "shelf life," making them impractical for diabetic treatment.

Scientists later discovered that, if zinc ions are added to the solution, the hI molecules tend to aggregate into hexameric association states, each containing six hI molecules and two zinc ions. In each association state, the zinc ions and the hI molecules are held together by weak intermolecular forces that are weaker than intramolecular covalent bonds. n3 Scientists have analyzed the conformation, or shape, of a Zn-hI hexamer and refer to the shape of this conformation as T[6]. When the hI molecules are in these hexamer association states, the rate at which hI molecules form polymers is much slower than the rate at which monomers of hI form polymers. Therefore, solutions of hI, where the most of the hI molecules are in hexamer association states, have a much longer shelf life than solutions of hI where most of the hI molecules are monomers.

n3 In contrast, the polymers of hI are held together by strong covalent bonds.

[*6]

Scientists next discovered that, if zinc ions and phenolic derivatives are added to the solution of pure hI, the hI molecules aggregate into slightly different hexamer association states, each containing six hI molecules, two zinc ions, and three or more phenolic molecules. The scientists analyzed the conformation of the Zn-phenolic-hI hexamer association state and discovered that it is different from the T[6] conformation of the Zn-hI hexamer association state. Scientists refer to the conformation of the Zn-phenolic-hI hexamer association state as R[6]. n4 The rate at which hI molecules in R[6] association states form polymers is about the same as the rate at which hI molecules in T[6] association states form polymers and is much slower than the rate at which monomers of hI form polymers. Therefore, solutions of

hI, where the most of the hI molecules are in R[6] association states, have a much longer shelf life than solutions of hi where most of the hI molecules are monomers.

n4 The hI molecules can also aggregate into a hybrid T[3]R[3] hexamer conformation, where three molecules of hI have a T conformation and three molecules of hI have a R conformation.

[*7]

However, hI molecules will only act in the bloodstream to transport sugar when they are monomers, and not aggregated into hexamers. Thus, when solutions containing T[6] or R[6] hexamers are injected into the body, the hexamers must disassociate, releasing monomers of hI into the bloodstream. Scientists discovered that the T[6] and R[6] hexamer association states take almost one hour to fully dissociate into monomers once injected into the body. Therefore, it is difficult for patients to time injections to coincide with the peaks of blood sugar after eating a meal.

To attempt to solve this problem, scientists developed human insulin analogs (hIA) which are hI molecules with one or more of the amino acids either altered or deleted. n5 The idea was to create hIA's that would perform the same blood sugar transport function as hI, but that would resist aggregation into hexamers so as to avoid the problem with long dissociation times. Scientists engineered at least twelve different hIA's that transport blood sugar as effectively as hI. As scientists predicted, these hIA molecules do not aggregate into stable hexamer association states either by themselves or in the presence of [*8] zinc ions. However, these hIA monomers have the same problem as monomers of hI. The molecules tend to rapidly form biologically inactive polymers. Thus, solutions of hIA monomers, like solutions of hI monomers, have a very short shelf life.

n5 The hIA's have special shorthand abbreviations. If an amino acid is substituted it is shown by the abbreviation of the new amino acid with its position as a superscript. For example, Asp<B28>-hI means that Asp has been substituted as a new amino acid at position 28 on the B chain. If an amino acid is deleted, it is represented by "des" followed by the position deleted. For example, des(B27)-hI means that the amino acid at position 27 in the B chain has been deleted.

B. The '978 Patent

The specification of the '978 patent teaches the following. The inventors sought to solve the problem of solutions of hIA monomers tending to rapidly form covalently bound polymers by trying to make hIA molecules aggregate into weakly bound, stable, hexameric association states. [*9] Scientists already knew that the hIA molecules would not aggregate into hexamers by themselves or in the presence of zinc ions. The inventors were able to make the hIA molecules form stable hexamer association states by adding both zinc ions and phenolics to solutions containing pure hIA.

Each hexamer association state is composed of six molecules of hIA, two zinc ions, and at least three molecules of phenolics, held together by weak intermolecular forces, weaker than covalent bonds. The inventors analyzed the conformation, or shape, of the Zn-phenolic-hIA hexamer association state and discovered that it is different from the T[6] conformation of the Zn-hI hexamer association state and the R[6] conformation of the Zn-phenolic-hIA hexamer association state.

Moreover, solutions containing mostly Zn-phenolic-hIA hexamers have all of the advantages of solutions containing mostly hI hexamers, without the disadvantages. The hIA molecules in the Zn-phenolic-hIA hexamers tend to form polymers at a very slow rate (about the same rate as hI molecules in T[6] and R[6] hexamers), giving the solution a long shelf life. Also, the Zn-phenolic-hIA hexamers tend to dissociate into monomers [*10] of hIA at a much faster rate than do the T6 and R6 hexamers of hI. Thus, solutions of hIA hexamers have more rapid action than solutions of hI hexamers.

The '978 patent has thirteen claims directed to this invention, three of which are independent. n6 Independent claims 1 and 12 claim a "human insulin analog complex." Dependent claims 2-8 claim a "parenteral pharmaceutical formulation comprising the human insulin analog complex of claim 1." Dependent claims 10-11 claim a method of using a "pharmaceutical formulation containing the composition of claim 1." Independent claim 13 claims a "parenteral pharmaceutical formulation."

n6 The full text of the claims is:

1. A human insulin analog complex, which comprises: six molecules of a human insulin analog, two zinc ions, and at least three molecules of a phenolic derivative selected from the group consisting of m-cresol, phenol, or a mixture of m-cresol and phenol; such that the insulin analog

complex is a hexamer; wherein the human insulin analog is human insulin wherein Pro at position B28 is substituted with Asp, Lys, Leu, Val, or Ala, and Lys at position B29 is Lys or Pro; des(B28-B30)-human insulin; or des (B27)-human insulin.

2. A parenteral pharmaceutical formulation comprising the human insulin analog complex of claim 1.

3. The parenteral pharmaceutical formulation of claim 2, which further comprises an isotonicity agent.

4. The parenteral pharmaceutical formulation of claim 3, which further comprises a physiologically tolerated buffer.

5. The parenteral pharmaceutical formulation of claim 4, wherein the buffer is sodium phosphate.

6. The parenteral pharmaceutical formulation of claim 5, wherein the isotonicity agent is glycerol.

7. The parenteral pharmaceutical formulation of claim 6, wherein the phenolic derivative is m-cresol.

8. The parenteral pharmaceutical formulation of claim 7, wherein the human insulin analog is Lys<B28>Pro<B29> -human insulin.

9. A human insulin analog composition of claim 1, wherein the human insulin analog is Lys<B28>Pro<B29>- human insulin.

10. A method of treating a patient suffering from diabetes mellitus, which comprises administering to said patient a pharmaceutical formulation containing the composition of claim 1.

11. The method of claim 10, wherein the human insulin analog is Lys<B28>Pro<B29> -human insulin.

12. A human insulin analog complex, consisting of: six molecules of insulin analog, two zinc ions, and at least three molecules of a phenolic derivative selected from the group consisting of m-cresol, phenol, or a mixture of m-cresol and phenol; such that the insulin analog complex is a hexamer; wherein the human insulin analog is human insulin wherein Pro at position B28 is substituted with Asp, Lye, Leu, Val, or Ala, and Lys at position B29 is Lys or Pro; des(B28-B30)-human insulin; or des(B27)-human insulin.

13. A parenteral pharmaceutical formulation consisting of: about 3.5 mg/mL Lys<B28>Pro<B29>-human insulin, about 19.7 mu g/mL, zinc, about 7 mM sodium phosphate, about 16 mg/mL glycerin, and about 29 mM m-cresol; wherein Lys<B28>Pro<B29>-human insulin is a hexamer.

[*11]

The following claim language is in dispute:

1. "human insulin analog complex" and "complex" (claims 1, 12);

2. "such that the insulin complex is a hexamer," "wherein Lys<B28>Pro<B29>-human insulin is a hexamer," and "hexamer" (claims 1, 12, 13);

3. "pharmaceutical formulation" (claims 2-11, 13);

4. "comprises" and "two zinc ions" (claim 1);

5. "consisting of" and "two zinc ions" (claim 12);

6. "wherein the human insulin analog is human insulin wherein Pro at position B28 is substituted with Asp, Lys, Leu, Val, or Ala, and Lys at position B29 is Lys or Pro; des(B28- B30)-human insulin; or des (B27)-human insulin" (claims 1, 12) and the T[6] limitation n7;

n7 *See, infra*, Section IV.E for an explanation of the T[6] limitation.

7. "hexamer" (claims 1, 12, 13) and the R[6] limitation n8;

8. "parenteral" (claims 2-11, 13);

9. "administering" (claim 10);

10. "patient" (claim 10).

n8 *See, infra*, Section IV.E for an explanation of the R[6] limitation.

[*12]

III. Applicable Law for Claim Construction

[HN1] Patent infringement actions are composed of two phases. First, in the claim construction, or *Markman*, phase, the court determines the scope and meaning of the patent claims as a matter of law. *See Cybor Corp. v. FAS Technologies, Inc.*, 138 F.3d 1448, 1454 (Fed. Cir. 1998)

(en banc) (citing *Markman*, 517 U.S. at 371-73). Second, the claims are compared to the allegedly infringing device. *See id.* In this opinion, the Court concerns itself only with the claim construction phase.

[HN2] The proper construction of claims is based primarily on the intrinsic evidence: the claim language, the specification, and the prosecution history. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1309 (Fed. Cir. 1999). n9 Claims should be construed from the point of view of the person of ordinary skill in the field of the invention at the time of the invention. *See Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998).

> n9 Patent claims "particularly point out and distinctly claim the subject matter which the applicant regards as his invention." *Markman*, 116 S. Ct. at 1387-88 (quoting 35 U.S.C. § 112). The patent specification "describes the invention 'in such full, clear, concise, and exact terms as to enable any person skilled in the art . . . to make and use the same.'" *Id.* at 1388. The prosecution history "contains the record of all the proceedings before the Patent and Trademark Office, including any express representations made by the applicant regarding the scope of the claims." *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).
>
> ----------End Footnotes----------

[HN3]

[*13]

The claim language itself is first and foremost in importance when construing the meaning and scope of the patent. *See Smiths Indus. Medical Systems, Inc. v. Vital Signs, Inc.*, 183 F.3d 1347, 1357 (Fed. Cir. July 14, 1999); *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 989 (Fed. Cir. 1999). [HN4] The general rule for interpreting the language of a claim is:

> that terms in the claim are to be given their ordinary and accustomed meaning. General descriptive terms will ordinarily be given their full meaning; modifiers will not be added to broad terms standing alone. In short, a court must presume that the terms in the claim mean what they say, and, unless otherwise compelled, give full effect to the ordinary and accustomed meaning of claim terms.

Johnson Worldwide, 175 F.3d at 989. Thus, if the claim is unambiguous and clear on its face, the Court need not consider the other intrinsic evidence. *See Smiths Indus.*, 183 F.3d at 1357 (citing *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1248-49 (Fed. Cir. 1998)).

[HN5] Where the applicability of a common meaning is unclear [*14] or where more than one common meaning could be assigned to a claim term, reference to the specification and prosecution history is appropriate to discern the ordinary and accustomed meaning. *See id.* at 1248; *Phillips Petroleum Co. v. Huntsman Polymers Corp.*, 157 F.3d 866, 871 (Fed. Cir. 1998) (turning to specification where, at time of invention, the ordinary meaning of term was disputed and two possible meanings were in existence). Thus, "the claims are construed in accordance with the rest of the specification of which they are a part, and not contrary to it." *C.R. Bard, Inc. v. M3 Systems*, 157 F.3d 1340, 1360 (Fed. Cir. 1998); *Renishaw*, 158 F.3d at 1250. Indeed, "the construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw*, 158 F.3d at 1250.

[HN6] A court engaging in claim construction may enter "a definition of a claim term other than its ordinary and accustomed meaning" in two situations. *Johnson Worldwide*, 175 F.3d at 990. "The first arises if the patentee has [*15] chosen to be his or her own lexicographer by clearly setting forth an explicit definition for a claim term" in the specification. *Id.* (citations omitted); *accord Renishaw*, 158 F.3d at 1249. "The second is where the claim term or terms chosen by the patentee so deprive the claim of clarity that there is no means by which the scope of the claim may be ascertained from the language used." *Johnson Worldwide*, 175 F.3d at 990 (citations omitted). "In these two circumstances, a term or terms used in the claim invites -- or indeed, requires -- reference to intrinsic [evidence beyond the claim language itself] or in some cases, extrinsic evidence to determine the scope of the claim language." *Id.* (citation omitted).

[HN7] The specification has been described as "often the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). When the specification explains and defines a term used in the claims, without ambiguity or incompleteness, there is no need to search further for the meaning of the term. *See Multiform Desiccants*, 133 F.3d at 1478. At the same [*16] time, however, a court "may not read a limitation into a claim from the written description." *Renishaw*, 158 F.3d at 1248; *see also Comark Communications, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186 (Fed. Cir. 1998).

In addition, [HN8] the prosecution history informs the understanding of terms found in both the specification and the claim. *See Multiform Desiccants*, 133 F.3d at 1478. ("The evolution of restrictions in the claims, in the course of examination in the PTO, reveals how those closest to the patenting process -- the inventor and the patent examiner -- viewed the subject matter."). "Use of the prosecution history to *interpret* claim language is distinct from prosecution history *estoppel*, which is a limitation on the doctrine of equivalents." 5A Donald S. Chisum, Chisum on Patents § 18.03[d][2] (1998) (emphasis in original); *see also Amhil Enterprises Ltd. v. Wawa, Inc.*, 81 F.3d 1554, 1559 (Fed. Cir. 1996). In most instances, the prosecution history is cited to refute an overly broad interpretation of a claim term put forth by the patentee. *See, e.g., Multiform Desiccants*, 133 F.3d at 1478. [*17]

[HN9] After examining the intrinsic evidence of the patent, if the meaning of the claim language is still ambiguous, the Court may consider extrinsic evidence, "if necessary to aid the court's understanding of the patent." *See Wright Medical Technology, Inc. v. Osteonics Corp.*, 122 F.3d 1440, 1443 (Fed. Cir. 1997). However, "if the meaning of a disputed claim term is clear from the intrinsic evidence -- the written record -- that meaning, and no other, must prevail; it cannot be altered or superseded by witness testimony or other external sources simply because one of the parties wishes it were otherwise." *Key Pharmaceuticals v. Hercon Labs. Corp.*, 161 F.3d 709, 716 (Fed. Cir. 1998). [HN10] The Federal Circuit has ranked four common forms of extrinsic evidence from most reliable to least reliable: (1) technical treatises and dictionaries; (2) prior art; n10 (3) expert testimony on technology; n11 and (4) expert testimony on claim construction. n12 *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584-85 (Fed. Cir. 1996). In some cases, reference to extrinsic evidence, although not necessary for claim construction, may have a useful confirmatory [*18] purpose. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999).

n10 The prior art can shed light on how terms have been used by those skilled in the art. *See Vitronics*, 90 F.3d at 1585.

n11 Expert testimony may help the court understand the underlying technology. *See id.*

n12 The opinions of experts and inventors on claim construction should be given little, if any, weight in claim interpretation. *See id.*

Finally, [HN11] if a claim term is still ambiguous, the court should adopt the interpretation that affords more narrow coverage of allegedly infringing devices, so that the claims perform their intended function of giving notice of what is covered to potential infringers. *See Athletic Alternatives, Inc. v. Prince Manufacturing, Inc.*, 73 F.3d 1573, 1581 (Fed. Cir. 1996).

IV. Claim Construction of the '978 Patent

A. Claims 1, 12, and 13 and the definitions of "complex," "hexamer," and "formulation"

Lilly argues [*19] that "complex" (claims 1 and 12) n13 means "an equilibrium of association species and their free constituents in solution." Docket Item ("D.I.") 156 at 2. It then argues that the terms "complex is a hexamer" (claim 1) and "LysPro-human insulin is a hexamer" (claim 13) mean "nearly all of the human insulin analog in the solution are in the hexameric association state." n14 D.I. 156 at 2. Lilly also maintains that the term "formulation" does not have any meaning independent of the term "pharmaceutical," *see* Transcript ("Tr.") at 390:24-391:16, and that the phrase "pharmaceutical formulation" (claim 13) means "an aqueous solution formulated to be of appropriate safety and efficacy for treatment of patients." n15 D.I. 156 at 2.

n13 Since claims 1 and 12 are identical, except for the use of "comprises" in claim 1 and "consisting of" in claim 12, the meaning of "complex," "hexamer," and "formulation" will be identical for purposes of both claims. *See Digital Biometrics Inc. v. Identix, Inc.*, 149 F.3d 1335, 1345 (Fed. Cir. 1998) (general rule is that same words in claims should be given same meaning). Therefore, for the remainder of the discussion of "complex," "hexamer," and "formulation," unless otherwise indicated, claim 1 will be used as the representative claim for claims 1 and 12. However, the Court notes that it departs from this general rule, as discussed *infra*, because the term "hexamer" means something different in claim 13 than it does in claims 1 and 12.

[*20]

n14 Lilly's exact argument is that "such that the insulin analog complex is a hexamer" means "an equilibrium of association species and their free constituents in solution where nearly all of the human insulin analog in the solution are in the hexameric association state." D.I. 156 at 2. When one removes the part of the definition that is identical to the definition of "complex," one is left with the definition of "hexamer" quoted in the text.

n15 The term "pharmaceutical" is discussed in Part IV.C, *infra.*

Novo first argues that "human insulin analog complex" (claim 1) means "a distinct arrangement of individual human insulin analog molecules that are associated or grouped together, with other individual components, all of which are in fixed numerical proportions with respect to each other." D.I. 154 at 25. It then argues that "complex" means "that the individual molecules come together or associate with each other to form a distinctive composition of matter or chemical species, also called an 'association state.'" D.I. 154 at 25. Novo contends that "hexamer" means "a distinct association [*21] of six molecules of one of the specified human insulin analogs, together with the specified two zinc ions and the specified at least three phenolic molecules, in a hexamer structure." n16 D.I. 154 at 28. Novo maintains that "pharmaceutical formulation" means "a composition that contains a medicinal drug or a biologically active agent and is suitable for administration to an animal." D.I. 154 at 33. However, Novo also implies that "formulation" alone refers to the equilibrium state. First, Novo argues that "complex" does not mean an equilibrium state because "complex is distinguished in the patent from formulations containing the complex." D.I. 172 at 7. Moreover, at the *Markman* hearing, Novo argued that "formulation" means "the equilibrium solution" or "putting it together in a solution or mixture," Tr. at 391:23-24.

n16 Novo further argues that the term "hexamer" contains a limitation that it is "not analogous to the R[6] hexamer of human insulin" ("the R[6] limitation"). D.I. 154 at 28. This limitation is discussed in Part IV.D, *infra.*

[*22]

Before discussing the merits of the respective definitions, it is helpful to discuss where the parties agree, and to define some short hand terminology that will make the discussion more concise. The following chemical equation summarizes how the individual molecules (or free constituents) of hIA, zinc, and phenolics come together to form a hexamer association state and shows the equilibrium between the individual molecules and the hexamer association state:

6 hIA + 2 Zn<+2> + 3 (or more) phenolic < -> (hIA)[6](Zn<+2>)[2](phenolic)[3] [(or more)]

[the individual molecules or free constituents] [the hexamer association state]

For convenience, the entire equilibrium between the individual molecules and the hexamer association state will be referred to as the "equilibrium," while each individual molecule or free constituent will be referenced by the general term "molecule." The term "molecular structure" will refer generally to any type of individual chemical association state of two or more molecules held together by non-covalent bonds. Finally, the individual molecular structure of six hIA molecules, two zinc ions, and at least three phenolics will be referred [*23] to as the "Zn-hIA structure."

Using this shorthand, Novo essentially argues that the term "complex" (claim 1) is a general term referring to any molecular structure and that "hexamer" (claims 1 and 13) refers to the Zn-hIA structure. Lilly agrees that individual molecules, molecular structures and Zn-hIA structures do exist. n17 However, Lilly argues that the term "complex" refers to the equilibrium containing molecules and molecular structures and that "complex is a hexamer" (claim 1) and "LysPro-human insulin is a hexamer" (claim 13) means that most of the species in the equilibrium are Zn-hIA structures. Novo agrees that an equilibrium exists and that the Zn-hIA structures exist as part of a larger equilibrium. n18 Indeed, Novo argues that "formulation" (claims 2-11 and 13) refers to the equilibrium containing the Zn-hIA structures. Thus, the parties agree that the molecular structures, Zn-hIA structures, and equilibrium exist. The dispute centers around whether the claim language is directed to a molecular structure or to an equilibrium.

n17 For example, Lilly's own definition of "is a hexamer" states that "most of the analog are in the hexameric association state" meaning that most of the hIA molecules are bound together with one another in Zn-hIA structures. D.I. 156 at 3. Also, Lilly's definition of "complex" as "equilibrium of association species and their free constituents in solution" means that the equilibrium contains many molecular structures. D.I. 156 at 2. In addition, in its Opening Brief Lilly argues that in the equilibrium, "nearly all the insulin analog molecules come together in six molecule units," which refers to molecular structures bonding together in Zn-hIA structures. See D.I. 156 at 8. Although Lilly argues that these structures exist nowhere in isolation, Lilly does not dispute that they do exist.

[*24]